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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
CHUNDURU, SURYAPRABHA	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 02/26/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/747,538	KATZ ET AL.	
	Examiner	Art Unit	
	Suryaprabha Chunduru	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *19 December 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *17,18 and 38-42* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17, 18, 38-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicants' response to the office action and amendment (Paper No. 14) filed on December 19, 2002 has been entered.

Response to Arguments

2. Applicant's response to the office action (Paper No.14) is fully considered and found persuasive in view of amendment and arguments.

3. With reference to the objection made in the previous office action, to the abstract of the instant specification, the objection is withdrawn herein, in view of Applicants' amendment (Paper No.14).

4. With reference to the rejection made in the previous office action under 35 USC 112 second paragraph, the rejection is withdrawn in view of the Applicants' amendment (Paper No. 14).

5. With reference to the rejection in the previous office action under 35 U.S.C. 102(b), applicants' arguments and amendment have been fully considered and the rejection is moot in view of the amendment and new grounds of rejection.

6. With reference to the rejection in the previous office action under 35 U.S.C. 103(a), applicants' arguments and amendment have been fully considered and the rejection is moot in view of the amendment and new grounds of rejection.

New grounds of Rejection

Claim Rejections - 35 USC § 112

7. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 42 provides for the use of the method in claim 38 to detect gene deletions or insertions in CYP2D6 locus, but, since the claim does not set forth any steps involved in the method/ process, it is unclear what method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced.

Claim 42 is rejected under 35 U.S.C. 101 because the claimed recitation of a use, without setting forth any steps involved in the process, results in an improper definition of a process, i.e., results in a claim which is not a proper process claim under 35 U.S.C. 101. See for example *Ex parte Dunki*, 153 USPQ 678 (Bd.App. 1967) and *Clinical Products, Ltd.* v. *Brenner*, 255 F. Supp. 131, 149 USPQ 475 (D.D.C. 1966).

Claim Rejections - 35 USC § 102

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
> (e) the invention was described in-
> (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effect under this subsection of a national application published under section 122(b) only if the international application designating the United States was published under Article 21(2)(a) of such treaty in the English language; or
> (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that a patent shall not be deemed filed in the United States for the purposes of this subsection based on the filing of an international application filed under the treaty defined in section 351(a).

A. Claims 17 and 18 are rejected under 35 U.S.C. 102(e) as being anticipated by Wittwer et al. (USPN. 6,232,079).

Wittwer et al. teach a method for detecting a target nucleic acid sequence in a test sample comprising (a) contacting the test sample with amplification reagents comprising a polymerase, a PCR primer pair, and a probe (see column 6, lines 1-15, column 44, lines 24-38); (b) performing

PCR cycles (i) raising temperature to dissociate the double-stranded genomic DNA, lowering the temperature to allow primers and probe to hybridize to the target nucleic acid, raising the temperature to dissociate the target-probe hybrids and extending the primers and continuously raising the temperature to temperature dependent polymerase extension (see column 44, lines 50-67, column 45, lines 1-12); (c) repeatedly performing the PCR cycles to form an amplification product (see column 45, lines 13-53) and (d) detection of the amplification product as an indication of presence of the nucleic acid (see column 45, lines 13-53). Wittwer et al. also disclose that the target nucleic acid sequence is a polymeric nucleic acid sequence (see column 44, lines 24-38). Thus the disclosure of Wittwer et al. meets the limitations in the instant claims.

B. Claims 17-18, 38-41 are rejected under 35 U.S.C. 102(e) as being anticipated by Lapidus et al. (USPN.6,143,529).

With reference to the instant claims 17 and 18, Lapidus et al teach a method for detecting a target nucleic acid sequence comprising (a) contacting a test sample with a probe, a pair of primers and amplification reagents (see column 10, lines 29-67); (b-c) performing repeated PCR cycles comprising raising temperature (denaturation cycle), annealing cycle, primer extension cycle followed by one cycle of primer extension (see column 11, lines 37-40); (d) detecting the amplification product as an indication of the presence of the nucleic acid in the test sample (see column 11, lines 64-67, column 12, lines 38-43). Lapidus also disclosed that the method comprises target nucleic acid comprising a ploymorphic nucleic acid sequence (see column 13, lines 8-52).

With reference to the instant claims 38-40, Lapidus et al. teach a method for detecting a deletion or insertion in a target nucleic acid suspected to have greater than 200bp long or less

than 200bp long (see column lines 36-51) wherein the method comprises (a and b) contacting a patient sample (test sample) comprising a known standard sequence and a sequence having suspected mutation with amplification reagents to form a reaction mixture and subjecting the reaction mixture to amplification conditions (see column 8, lines 54-67, column 9, lines 1-67, column 10, lines 1-67, column 11, lines 37-67, column 12, lines 38-43); (c) detecting a first signal proportional to the amount of target nucleic acid (see column 13, lines 55-67, column 14, lines 1-49); (d) detecting a second signal that is proportional to the amount of the standard nucleic acid amplification product (column 12, lines 38-67, column 13, lines 1-14); (e) comparing the said amount of DNA in the sample with that of a standard nucleic acid and determining whether a deletion or insertion of greater or less than 200 bp is present in the test sample (see column 8, lines 4-13). Lapidus et al. discloses the mutation includes less than or greater than 200bp which includes the limitation in the instant claims 38-40.

With reference to the instant claim 41, Lapidus et al. disclose that the method comprises amplification conditions of the instant claim 17 (see column 10, lines 29-67, column 11, lines 37-67, column 12, lines 38-43). Thus the disclosure of Lapidus et al. meets the limitations in the instant claims.

Claim Rejections - 35 USC § 103

9. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Lapidus et al. (USPN.6,143,529) and in view of Johansson et al. (Pharmacogenetics, Vol. 6, pp. 351-355, 1996).

Lapidus et al teach a method for detecting a target nucleic acid sequence comprising (a) contacting a test sample with a probe, a pair of primers and amplification reagents (see column 10, lines 29-67); (b-c) performing repeated PCR cycles comprising raising temperature (denaturation cycle), annealing cycle, primer extension cycle followed by one cycle of primer extension (see column 11, lines 37-40); (d) detecting the amplification product as an indication of the presence of the nucleic acid in the test sample (see column 11, lines 64-67, column 12, lines 38-43). Lapidus also disclosed that the method comprises target nucleic acid comprising a ploymorphic nucleic acid sequence (see column 13, lines 8-52). Lapidus et al. also teach a method for detecting a deletion or insertion in a target nucleic acid suspected to have greater than 200bp long or less than 200bp long (see column lines 36-51) wherein the method comprises (a and b) contacting a patient sample (test sample) comprising a known standard sequence and a sequence having suspected mutation with amplification reagents to form a reaction mixture and subjecting the reaction mixture to amplification conditions (see column 8, lines 54-67, column 9, lines 1-67, column 10, lines 1-67, column 11, lines 37-67, column 12, lines 38-43); (c) detecting a first signal proportional to the amount of target nucleic acid (see column 13, lines 55-67,

column 14, lines 1-49); (d) detecting a second signal that is proportional to the amount of the standard nucleic acid amplification product (column 12, lines 38-67, column 13, lines 1-14); (e) comparing the said amount of DNA in the sample with that of a standard nucleic acid and determining whether a deletion or insertion of greater or less than 200 bp is present in the test sample (see column 8, lines 4-13). Lapidus et al. discloses the mutation includes less than or greater than 200bp which includes the limitation in the instant claims 38-40. However, Lapidus et al. did not teach detection of gene deletions or insertions in CYP2D6 locus.

Johansson et al. teach a method for distinguishing the presence of a target nucleic acid and a variant which comprises a deletion (deletion of entire coding region (CYP2D6*5)), wherein Johansson et al. disclose that the method comprises contacting a test sample (containing DNA) with amplification reagents and a first and second amplification primer specific for the target site, subjecting the reaction mixture to amplification conditions, and detecting the amplification product as an indication of the presence of the target nucleic acid sequence (see page 351, column 1, paragraph 1, and page 353, column 2, paragraph 1). Johansson et al. also teach that the method could be used to alter drug therapy (patient's care) and for evaluating the linkage between the CYP2D6 genotype and disease and aid in drug development (see page 354, column 2, paragraph 1).

Therefore, it would have been prima facie obvious to a person of ordinary skill in the art at the time the invention was made, to modify a for detecting a deletion or insertion as taught by Lapidus et al. with a method for detecting a variant (CYP2D6 gene deletion) as taught by Johansson et al. to achieve expected advantage of developing a method for enhanced sensitivity of detecting a target nucleic acid and its variant because Johansson et al. states that "it was

considered of importance to develop simple PCR-based methods that could be used for efficient genotype analysis of ultrapid metabolizers" (see page 351, column 2, lines 15-18). An ordinary practitioner would have been motivated to combine the method of Lapidus et al. with the method of Johansson et al. in order to achieve the expected advantage of developing a sensitive method for amplification based detection of target nucleic acid.

Conclusion

No claim is allowable.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Suryaprabha Chunduru whose telephone number is 703-305-1004. The examiner can normally be reached on 8.30A.M. - 4.30P.M, Mon - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on 703-308-1119. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and - for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Suryaprabha Chunduru
February 20, 2003

JEFFREY FREDMAN
PRIMARY EXAMINER